REMARKS

Claims 1, 3, 5-6, 12, 15, and 21-45 have been canceled solely to comply with the Office's restriction requirement. The claims have been canceled without disclaimer of any subject matter contained therein. The right to file subsequent applications covering that matter is reserved.

Pending claims 4, 7-10, 11, 13, 14, and 16-20 have also been canceled. These claims have been re-written as new claims 46, 47-50, 51, 52, 53, 54-58, respectively. The claims were re-written solely to comply with U.S. claiming practice.

Further support for the new claims can be found throughout the specification including the claims as filed originally. For instance, specific support for reciting a "therapeutically effective amount" of the GPI-PLD enzyme can be found at pg. 24.

New claims 58-59 and 67 find particular support at pg. 7, line 34 to pg. 8, line 2 (specifying that septic shock embodiments can be treated be GPI-PLD).

New claims 60-67 are also well-supported by the specification as filed originally. For instance, use of particular enzyme fragments is disclosed at pg. 17, lines 31-32 to pg. 18, line 16 (disclosing the N-terminal 39kD portion of GPI-PLD as active, for example). Additional support can be found at pgs. 11-12, bridging paragraph, and pg. 44, lines 4-20 (providing for use of a specific GPI-PLD variant having reduced phosphorylation detectable by mass spectrometry). New claim 66 enjoys specific support from pgs. 18-19, bridging paragraph.

No new matter has been added by virtue of the new claims.

Oath/Declaration

The USPTO took the position that the previously filed oath or declaration was defective. A fresh oath/declaration is attached to this submission that should address these concerns.

Sequence Compliance

The Office took the position that Figures 1-8 are not identified by sequence identifier numbers. The Examiner suggested that it would be remedial to submit new Drawings with sequence identifiers. To comply, Applicants have attached new Drawings for review by the Examiner. The Drawings have been revised merely to comply with the Office's sequence listing requirement. No new matter has been added.

Claim Objections

Claims 11 and 16 (now canceled) were objected to for alleged multiple dependency. The objection is moot in view of this submission.

35 USC §101

Claims 4, 7-10, 13-14, and 17-20 stand rejected under §101. The claims have been canceled and re-written as new claims 46, 47-50, 51, 52, 53, 54-58 merely to comply further with acceptable USPTO claim drafting practice.

Reconsideration and withdrawal of the rejection are respectfully requested.

35 USC §112, second paragraph

Claims 4, 7-10, 13-14, and 17-20 stand rejected as being unclear on various grounds. The claims have been canceled in favor of new claims 46, 47-50, 51, 52, 53, 54-58. Accordingly, the rejection is moot and reconsideration is requested.

35 USC §112, first paragraph

Claims 4, 7-10, 13-14, and 17-20 stand rejected as failing to comply with the enablement requirement set forth by §112, first paragraph. The rejection is moot in view of the present submission (the claims are canceled). However, Applicants wish to respond in view of the corresponding pending claims 46, 47-50, 51, 52, 53, 54-58. To the extent the rejection would be applied to those claims, Applicants respectfully disagree.

In support, Applicants submit the attached Declaration of Thomas Rademacher ("hereinafter Declaration"). The Declaration shows, for instance, that in view of the guidance provided by the instant specification, a worker in the field would know how to use the GPI-PLD enzyme to treat diseases such as diabetes and hypoglycemia. No undue experimentation is required. Accordingly, reconsideration and withdrawal of the enablement rejection are requested.

Turning to the Declaration, it establishes, among other things, that Dr. Rademacher is a Professor of Molecular Medicine in the Department of Immunology and Molecular Pathology, Division of Infectious Diseases, at University College of London, England. Decl. at ¶¶ 1-2. It further establishes that Dr. Rademacher is a co-inventor of the subject application and pending claims. Decl. at ¶ 3. Dr. Rademacher further states that he read the instant Office Action and understands it but that he disagrees with the enablement rejection. Decl. at ¶ 4.

Applicants submit that the enablement rejection cannot withstand scrutiny, particularly to the extent it relies on the cited Torchilin and Meng references. See pgs. 8-9 of the Action (citing the references as evidence that the field of the invention is unpredictable). Reconsideration is respectfully requested.

For instance, and as Dr. Rademacher makes clear, the Torchilin reference does not specifically exclude use of glycosyl phosphatidyl inositol specific phospholipase D (GPI-

PLD) according to the claimed methods. Decl. at ¶¶ 5-7. Further, Dr. Rademacher stated that as he understands the reference, it discloses successful use of certain peptides and antibodies as promising therapeutics. Decl. at ¶ 7. Thus, to the extent the outstanding rejection relies on Torchilin it cannot stand

Further, the cited Meng reference also does not exclude use of GPI-PLD in the claimed methods according to Dr. Rademacher. Decl. at ¶ 8. Indeed, as he understands the reference, it relates to the field of using certain viruses to deliver anti-cancer therapeutics. Decl. at ¶ 8. That information, according to Dr. Rademacher, is not at all related to the field of the invention. Decl. at ¶ 8. To the extent Meng is relied on to substantiate the rejection, it cannot stand.

For these reasons alone, reconsideration and withdrawal of the enablement rejection are requested. The rejection, as currently formulated, does not establish that the field of the invention is unpredictable.

At pg. 9 of the Action, first full paragraph, the Office referenced the "Bent" reference. However, no citation has been provided and Applicants cannot review the reference. Clarification is respectfully requested. To the extent the rejection is based on the Bent reference it is improper and should be reconsidered.

In sum, the instant enablement rejection cannot withstand scrutiny to the extent it relies on the cited Torchilin, Meng and Bent references. The Torchilin and Meng references, as understood by Dr. Rademacher, simply do not support the assertion that the field of the invention is unpredictable Decl. at ¶ 9. As cited, Bent does nothing to support that rejection.

Applicants respectfully disagree with the enablement rejection on further grounds.

For instance, the instant specification satisfies the "how to make" and "how to use" requirement of §112, first paragraph. See Decl. at ¶¶ 10-16.

In support, Dr. Rademacher stated at ¶ 11 of the Decl. that he is familiar with unpublished research conducted along lines of the instant patent specification. It showed, for instance, that administration of GPI-PLD lowered plasma insulin and raised blood glucose in hyperinsulinaemic and insulin-resistant mice. Decl. ¶ 11. According to Dr. Rademacher, the mice were recognized animal models of human disease. Decl. ¶ 11. Moreover, he stated that the insulin and glucose changes he saw in the mice are highly significant and indicative of a new and useful therapeutic approach for the treatment of diabetes, hypoglycemia and related complications. Decl. ¶ 11.

As pointed out by Dr. Rademacher, the specification provides guidance about how to use the GPI-PLD enzyme to treat an animal including particular injection routes. Decl. ¶ 12. See the specification at pgs. 20-24, for instance (disclosing isotonic saline injection, for instance).

At ¶ 13 of the Declaration, Dr. Rademacher pointed out that a worker reading his patent specification would understand that how much GPI-PLD to administer would vary depending on recognized parameters eg., the severity of the disease and particular administration route selected. Taking diabetes as an example, Dr. Rademacher stated that a worker reading the specification would know that the disease varies somewhat among patients. Decl. ¶ 13. However, he also stated that with this knowledge in hand and in view of the guidance provided by the specification, the worker would know how to administer the GPI-PLD enzyme as a disease treatment. Decl. ¶ 13.

Referring more specifically to the unpublished research, Dr. Rademacher stated that administration of the GPI-PLD enzyme decreased plasma insulin in an accepted murine model of diabetes. Decl. ¶ 14 and Appendix A. This unpublished research showed, for

instance, that the GPI-PLD enzyme is a highly useful anti-diabetic agent. The administration route selected is in line with guidance provided by the patent specification. See the specification at pgs. 20-24, for instance.

Dr. Rademacher also stated that administration of GPI-PLD substantially increased blood glucose in the ob/ob mice. Decl. ¶ 15 and Appendix B. This unpublished research showed, for instance, that GPI-PLD is a useful agent for the treatment of hypoglycemia. The administration route selected is in accord with guidance provided throughout the patent specification. See eg., pgs. 20-24.

Dr. Rademacher concluded in his Declaration at ¶ 16 that the data provided by Appendices A and B show, for instance, that information provided by the specification can be used by a worker to treat indications characterized by reduced levels of the GPI-PLD enzyme (e.g., diabetes, related complications, liver dysfunction and disorders involving pancreatectomies). Dr. Rademacher stated that the information is completely consistent with the guidance provided by his patent specification. Decl. at ¶ 16. For instance, see the section under "Summary of Invention", pg. 20, line 33 to pg. 24, line 20; pg. 23, lines 30-33; and pg. 24, lines 1-20.

In sum, the instant patent specification fully satisfies the "how to make" and "how to use" requirements of §112, first paragraph. Dr. Rademacher has confirmed that the claimed invention can be used to treat diseases as set forth in the specification. Thus, concerns raised in the Action regarding an alleged lack of guidance about how to use GPI-PLD enzyme and whether the enzyme would work at all are not relevant to the issue of enablement. Applicants have clearly shown that the specification provides ample guidance for one working in this field to practice the claimed methods. No undue experimentation would be required to use the invention as claimed.

Accordingly, reconsideration and withdrawal of the §112 rejection are respectfully requested.

Applicants acknowledge that the present submission includes an unsigned Declaration. A signed version will follow under separate cover.

Although it is not believed that any additional fees are needed to consider this submission, the Examiner is hereby authorized to charge our deposit account no. **04-1105** should any fee be deemed necessary.

Respectfully submitted,

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